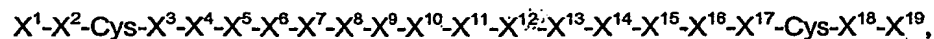


Claims

1. A peptide having a sequence of at most 44 amino acid residues comprising a motif of the formula



wherein

- X can be an amino acid sequence or a single amino acid residue selected either from Group 1 consisting of Ala, Gly, and Ser;

Group 2 consisting of Arg and Lys,

Group 3 consisting of His, Ile, Leu, Met, Phe, Pro, Thr, Val, Trp, and Tyr,

Group 4 consisting of Asn and Gln, or

- Group 5 consisting of Ala, Asn, Arg, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, Val,

wherein

X¹ can be represented by a sequence consisting of 2-5 amino acid residues or an amino acid residue selected from Group 2;

- X² is selected from Group 5 or Group 3;

X³, X¹⁵ and X⁴ are selected from Group 1;

X⁵ is Thr or selected from Group 1;

X⁶, X¹¹, X¹², X¹³ and X⁷ are selected from Group 3;

X⁸ and X¹⁷ are selected from Group 1, 3 or 4;

- X⁹ is selected from Group 5, 1 or 3;

X¹⁰ is selected from Group 2, 3 or 4;

X¹⁴ is Ser or selected from Group 3;

X¹⁶ and X¹⁸ is selected from Group 1 or 3

- X¹⁹ can be represented by a sequence consisting of 2-5 amino acid residues or a single amino acid residue selected from Group 5, 2, or 4,

with the proviso, that when X¹ includes Pro, then X¹⁹ is Gln.

2. The peptide according to claim 1, wherein X^1 is represented by an amino acid sequence selected from SEQ ID NOS: 607-612.
3. The peptide according to claim 1 or 2, wherein X^1 is Arg.
- 5 4. The peptide according to any of the claims 1-5, wherein X^2 is Phe.
5. The peptide according to any of the claims 1-6, wherein X^3 is Ala or Gly.
6. The peptide according to any of the claims 1-7, wherein X^4 is Gly.
- 10 7. The peptide according to any of the claims 1-8, wherein X^5 is Ala.
8. The peptide according to any of the claims 1-9, wherein X^6 is Leu.
- 15 9. The peptide according to any of the claims 1-10, wherein X^7 is Ile, Leu, Met or Val.
10. The peptide according to any of the claims 1-11, wherein X^8 is His or Val.
- 20 11. The peptide according to any of the claims 1-12, wherein X^9 is Ala, Phe or Pro.
12. The peptide according to any of the claims 1-13, wherein X^{10} is Arg.
13. The peptide according to any of the claims 1-14, wherein X^{11} is Phe or Pro.
- 25 14. The peptide according to any of the claims 1-15, wherein X^{12} is His or Val.
15. The peptide according to any of the claims 1-16, wherein X^{13} is Ile, Leu, Met or Val.
- 30 16. The peptide according to any of the claims 1-17, wherein X^{14} is Thr.
17. The peptide according to any of the claims 1-18, wherein X^{15} is Ala.
- 35 18. The peptide according to any of the claims 1-19, wherein X^{16} is Ala.

BEST AVAILABLE COPY

19. The peptide according to any of the claims 1-20, wherein X¹⁷ is Ser.

20. The peptide according to any of the claims 1-21, wherein X¹⁸ is Phe.

5

21. The peptide according to any of the claims 1-22, wherein X¹⁹ is a sequence identified as SEQ ID NO: 613

10

22. The peptide according to claims any of the claims 1-23, wherein X¹⁹ is Arg or Gln.

23. The peptide according to claim 3, wherein the N-terminal of the polypeptide chain is modified.

15

24. The peptide according to claim 4, wherein the N-terminal amino group is acetylated.

25. The peptide according to claim 24, wherein the C-terminal of the polypeptide chain is modified.

20

26. The peptide according to claim 25, wherein the C-terminal carboxy group is amidated.

25

27. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRHFCCGGALIHARFVMTAASCFR (SEQ ID NO: 595).

28. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRPFCCGGALIHARFVMTAASCFR (SEQ ID NO: 596).

30

29. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRHFCCGGALIHPRFVMTAASCFR (SEQ ID NO: 597).

30. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRPFCCGGALIHPRFVMTAASCFR (SEQ ID NO: 598).

35

BEST AVAILABLE COPY

31. The peptide according to any of the claims 1-26, wherein said peptide has the sequence RFCSAATLVFRPHVLGACFPRGQK (SEQ ID NO: 599).
- 5 32. The peptide according to any of the claims 1-26, wherein said peptide has the sequence NQGRPFCAGALVHPRFVLTAASCFR (SEQ ID NO: 600).
33. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRPFCAGALVHPRFVLTAASCFQ (SEQ ID NO: 601).
- 10 34. The peptide according to any of the claims 1-26, wherein said peptide has the sequence NQGRPFCAGALVHPRFVLTAASCFQ (SEQ ID NO: 602).
35. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRPFCAGALVHPQFVLTAASCFR (SEQ ID NO: 603).
- 15 36. The peptide according to any of the claims 1-26, wherein said peptide has the sequence LRGGHFCGATLIAPNFVMSAAHCVA (SEQ ID NO: 604).
37. The peptide according to any of the claims 1-26, wherein said peptide has the sequence RRGHFCGATLIARNFVMSAVHCVN (SEQ ID NO: 605).
- 20 38. The peptide according to any of the claims 1-26, wherein said peptide has the sequence RSREYRCGGTLVSQRYILTAASCAA (SEQ ID NO: 606).
- 25 39. The peptide according to any of the claims 1-26, wherein said peptide has the sequence NQGRHFCGGALIHARFVMTAASCFQ (SEQ ID NO: 594).
40. The peptide according to any of the claims 1-26, wherein said peptide has the sequence KQGRPFCAGALVHPRFVLTAASCFR (SEQ ID NO: 593).
- 30 41. The peptide according to claim 39 or 40, wherein the C-terminal carboxy group of said peptide is amidated and/or the N-terminal amino group is acetylated.

BEST AVAILABLE COPY

42. The peptide according to claim 1, wherein the motif comprises a sequence of the formula Cys-X₍₁₁₎-Ala-Ala-Ser-Cys, wherein X₍₁₁₎ represents a contiguous sequence of 11 amino acids.
- 5 43. The peptide according to claims 1, 2, or 42, wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 12-39.
44. The peptide according to claims 1-26 or 42 wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 233-253.
- 10 45. The peptide according to claims 1-26 or 42 and 44, wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 233-253 and SEQ ID NO: 34.
- 15 46. The peptide according to claims 1-26 or 42 and 44-45, wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 233-253 and SEQ ID NO: 21.
- 20 47. The peptide according to claims 1-26 or 42 and 44-45, wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 233-253 and SEQ ID NO: 21 and SEQ ID NO: 34.
- 25 48. The peptide according to claims 1-26 and 42, wherein the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 395-421.
49. The peptide according to claims 1-26 and 42, wherein the one or more amino acid sequences are derived from the sequence of human heparin-binding protein (hHBP) set forth in SEQ ID NO: 1.
- 30 50. The peptide according to claims 1-26 and 42, wherein the one or more amino acid sequences are derived from the sequence of porcine heparin-binding protein (pHBP) set forth in SEQ ID NO: 588.

BEST AVAILABLE COPY

51. The peptide according to claims 1-26 and 42, wherein the one or more amino acid sequences are derived from the sequence of human neutrophil elastase set forth in SEQ ID NO: 589.
- 5 52. The peptide according to claims 1-26 and 42 comprising one or more amino acid sequences set forth in SEQ ID NOS: 2-587.
53. The peptide according to any of the claims 1-52, wherein said peptide is capable of inhibiting the secretion of cytokine IL-6 from monocytes.
- 10 54. The peptide according to any of the claims 1-52, wherein said peptide is capable of stimulating the secretion of cytokine IL-6 from monocytes.
55. A process for the production of a peptide as defined in any of the claims 1-54, comprising the steps of
- 15 a) providing an expression vector containing a DNA sequence encoding one or more of the amino acid sequences as defined in the claims 1-54,
- 20 b) transforming host cells with the vector of step (a);
- c) culturing the transformed cells of step (b);
- d) purifying the expressed peptide.
- 25 56. The process according to claim 55, wherein the host cells are selected from the group comprising recombinant bacterial, yeast, insect or mammalian cells.
57. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the treatment of Gram negative bacterial infection.
- 30 58. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the treatment of Gram positive bacterial infection.
- 35

BEST AVAILABLE COPY

59. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the treatment of sepsis, severe sepsis, septic shock and disseminated intravascular coagulation.

5

60. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the treatment of meningitis.

61. The use according to claim 58, wherein meningitis is meningococcal meningitis.

10

62. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the treatment of pneumonia.

63. The use according to claim 60, wherein pneumonia is pneumococcal pneumonia.

15

64. Use of one or more peptides as defined in any of the claims 1-52 and 54 for the manufacture of a medicament for the stimulation of inflammatory response.

20

65. Use of one or more peptides as defined in any of the claims 1-53 for the manufacture of a medicament for the inhibition of inflammatory response.

66. Use of one or more peptides as defined in any of the claims 1-54 for the manufacture of a medicament for the prevention of cell apoptosis.

25

67. Use of a peptide comprising two or more sequences set forth in SEQ ID NOS: 20-36, wherein said sequences constitute a contiguous sequence derived from the sequence of human HBP set forth in SEQ ID NO:1 for the manufacture of a medicament for the treatment of individuals having suppressed immune system, cancer, auto-immune diseases and/or trauma.

30

68. The use according to claim 67, wherein the peptide is having the sequence identified in SEQ ID NO: 594, fragments, or variants thereof.

BEST AVAILABLE COPY

69. The use according to claim 68, wherein the peptide has the N-terminal amino group acetylated and/or C-terminal carboxy group amidated.

5 70. Use of a peptide comprising the sequence comprises one or more amino acid sequences are selected from SEQ ID NOS: 233-253 and SEQ ID NO: 21 and SEQ ID NO: 34, wherein said sequences constitute a contiguous sequence derived from the sequence of porcine HBP set forth in SEQ ID NO: 588 for the manufacture of a medicament for the treatment of individuals to suppress a sustained inflammatory response.

10 71. The use according to claim 70, wherein the peptide is having the sequence identified in SEQ ID NO: 593, fragments, or variants thereof.

15 72. The use according to claim 71, wherein the peptide has the N-terminal amino group acetylated and/or C-terminal carboxy group amidated.

73. A pharmaceutical composition comprising a peptide as defined in claims 1-54.

BEST AVAILABLE COPY